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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,866	07/02/2002	Michael Schimer	SCH 1869	6769

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EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 02/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,866	SCHIRNER ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/3/06 has been entered.

The rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of applicant's amendments.

The objection to the specification is withdrawn in view of applicant's amendment.

Information Disclosure Statement

The IDS filed 1/3/06 has been considered and an initialed copy of the PTO-1449 is enclosed.

Response to Arguments/New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claim 16 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of hybridoma cell lines producing L19 and E1. It is not clear that hybridomas possessing the identical properties of the aforementioned hybridomas are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a monoclonal antibody and hybridoma identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed monoclonal antibodies, a suitable deposit for patent purposes, evidence of public availability of the claimed L19 and E1 or evidence of the reproducibility without undue experimentation of the claimed antibodies, is required.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Response to Applicant's Arguments

Applicant states that in view of the Viti reference L19 is known in the art. The rejection is based upon being known in the art **and** public availability. Just because L19 in known in the art does not mean that it is readily available to the public.

Applicant did not address the public availability of E1.

Claims 15-33 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The reasons for this rejection are of record in the paper mailed 9/1/05.

With respect to "Y", applicant argues that they do specifically point to the portion that is relevant and cites page 9 of the specification "polymethine dyes, such as dicarbocyanine, tricarbocyanine, merocyanine and oxonol dyes (WO96/17262)". Licha US 6083485 is the English equivalent of the WO document. Applicant further states that the cyanine dyes and the merocyanine dyes are incorporated from Licha. The quoted statement above only provides support for incorporation of the specifically cited dyes and none other. Therefore the broad scope of cyanine and merocyanine dyes cannot be incorporated into the instant application. If applicant believes that only the specifically mentioned dyes have been incorporated, then applicant is invited to show (using structures) the correlation between the structure in the patent to that which is incorporated into the instant specification.

Applicant did not address the second part of this rejection (which is re-iterated below):

Second, the new limitations in claims 26 and 31 is new matter. The examiner was unable to the use of the claimed dyes in a method that included both intraoperative visualization and surgery.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-25, 27-30 and 32-33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97) in view of Viti et al Cancer Research vol. 59 p. 347 (1/99), applicant's admission in the sentence briding pages 7-8 of the specification and Licha et al US 6083485 (filed 11/7/97). This rejection has been modified to include antibody E1.

Neri et al discloses making and using scFv(CGS-1) labeled with infrared fluorophore CY and the use of this antibody-dye conjugate to detect blood vessels and to image tumors (reads on using in a pharmaceutical composition) in tumors by fluoresce microscopy (see page 1272 and 1273). ScFv is directed to ED-B fibronectin, which as is also known as oncofetal fibronectin (see abstract).

The only difference between the instant invention and the reference is the cyanine dyes and the use of L19 or E1.

Viti et al discloses that antibody L19 and E1 can be used in vivo to target new forming blood vessels of F9 teratocarcimona(page 349 (second column)) and that these antibodies have increased binding affinity.

Licha et al disclose a protein-dye conjugate wherein the dye is "F" (col. 4-5) and the a cyanine dye of the formula IIa. This formula reads on applicant's formula in claim 15. The dyes of this reference are irradiated with light from the visible to near infrared range from 650-1200 nm (see abstract and claims and column 8, lines 42-50).

Additionally in the sentence bridging pages 7-8 of the specification, applicant admits that "both macroscopic and microscopic detection are possible" using dyes in the near infrared range.

Since Licha et al discloses protein-dye conjugates using cyanine dyes and the use of these dyes in in vivo diagnostics, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the dyes of the secondary reference in place of the dyes of the primary reference with the expected benefit of achieving a conjugate that can be used in vivo diagnostic assays and with the expected benefit that the conjugate "accumulates in the edge area of the cell tissue of a focus of disease" making the edge area of the focus of disease optically detectable. In view of the fact that L19 and E1 can target newly formed blood vessels (reads on the edge area) in vivo and have increased binding affinity, it also would have been obvious to use L19 or E1 in the conjugate of the primary reference with the expected benefit of achieving an antibody-dye conjugate with higher binding affinity. Since both macroscopic and microscopic detection are possible using dyes in the near infrared range it also would have been obvious to use either detection method when using the protein-dye conjugates.

Response to Applicant's Arguments

Applicant argues that the references do not teach accumulation in the edge areas. The Viti et al reference discloses that the antibodies target new forming blood vessels. One of ordinary skill in the art would readily recognize that the new formations would be at an edge and not in the middle of an already formed vessel. Furthermore, the Viti et al reference is using the same antibodies as used by applicant. To this, applicant argues that the claims are directed to the combination of the dye and antibody not just antibody. It appears that applicant is suggesting that the binding of the

antibody-dye conjugate to the edge area is due the dye and that the dye has unique abilities to localize the conjugate to the edge area. This is merely an assertion and there is no objective evidence to support this. It is well established that binding of an antibody conjugate to its target is through the antibody. Furthermore, Viti et al disclose that it is the antibody L19 and E1 that bind to the new formed vessels. Thus it is clear that binding of the conjugate is through the antibody and not the dye.

Claims 15-25, 27-30 and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al WO 99/58570 (published 11/18/99) in view of applicant's admission in the sentence bridging pages 7-8 of the specification and Licha et al US 6083485 (filed 11/7/97). Applicant should note that the WO was filed between the filing date of the foreign priority document and the PCT. A perfected copy of the foreign document may help overcome this rejection.

Neri et al discloses making and using monoclonal antibody L19 chemically coupled to the red fluorophore Cy5 and that this conjugate targets ocular angiogenesis in vivo and subsequent ex vivo immunofluorescent microscopic analysis disclose that the localization was around the vascular structures (page 22, lines 15+). The reference also discloses that the L19 antibody localizes to newly formed blood vessels and that the new ocular vessels can be distinguished from the pre-existing ones using L19 (page 9, lines 18+). This reference also discloses that antibody E1 is the antibody that L19 was derived from.

The only difference between the instant invention and the reference is the cyanine dyes.

Licha et al disclose a protein-dye conjugate wherein the dye is "F" (col. 4-5) and the a cyanine dye of the formula IIa. This formula reads on applicant's formula in claim 15. The dyes of this reference are irradiated with light from the visible to near infrared range from 650-1200 nm (see abstract and claims and column 8, lines 42-50).

Additionally in the sentence bridging pages 7-8 of the specification, applicant admits that "both macroscopic and microscopic detection are possible" using dyes in the near infrared range.

Since Licha et al discloses protein-dye conjugates using cyanine dyes and the use of these dyes in in vivo diagnostics, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the dyes of the secondary reference in place of the dyes of the primary reference with the expected benefit of achieving a conjugate that can be used in vivo diagnostic assays. Because the conjugate would specifically bind to newly formed vessels and not pre-existing ones, this reads on recognizing the edge of the vessel. In view of the fact that L19 is derived from E1 and since L19 can target newly formed blood vessels in vivo, it also would have been obvious to use L19 or E1 in the conjugate of the primary reference. Since both macroscopic and microscopic detection are possible using dyes in the near infrared range it also would have been obvious to use either detection method when using the protein-dye conjugates.

Specification

The amendment filed 1/3/06 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendments starting at page 9, line 6 and the amendments starting at page 11, line 3. These portions were incorporated by reference to WO 96/17628. Specifically, page 9 of the specification recites "polymethine dyes, such as dicarbocyanine, tricarbocyanine, merocyanine and oxonol dyes (WO96/17262)". Licha US 6083485 is the English equivalent of the WO document. Applicant further states that the cyanine dyes and the merocyanine dyes are incorporated from Licha. The quoted statement above only provides support for incorporation of the specifically cited dyes and none other. Therefore the broad scope of cyanine and merocyanine dyes cannot be incorporated into the instant application. If applicant believes that only the specifically mentioned dyes have been incorporated, then applicant is invited to show (using structures) the correlation between the structure in the patent to that which is incorporated into the instant specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesdays and Thursdays from 5:30am to 2:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheela J Huff
Primary Examiner
Art Unit 1643

sjh